II. CLAIM AMENDMENTS

What is claimed is:

Claims 1-65 (Cancelled)

Claim 66 (Currently Amended) A compound of the formula

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$$A^{1}-Z^{2}-Z^{1}$$

$$R^{c}$$

$$X^{1}$$

$$X^{2}$$

$$X^{2}$$

$$(CH_{2})_{n}COR^{b}$$

or a pharmaceutically acceptable salt thereof, wherein



is a 4-8 membered monocyclic ring or 7-12 membered bicyclic ring; which ring is optionally saturated or unsaturated, which ring is optionally substituted with one or more substituent selected from the group consisting of alkyl, haloalkyl, aryl, heteroaryl, halogen, alkoxyalkyl, aminoalkyl, hydroxy, nitro, alkoxy, hydroxyalkyl, thioalkyl, amino, alkylamino, arylamino, alkylsulfonamide, acyl, acylamino, alkylsulfone, sulfonamide, allyl, alkenyl, methylenedioxy, ethylenedioxy, alkynyl, carboxamide, cyano, and -(CH₂)_m COR;

m is 0 to 2;

R is hydroxy, alkoxy, alkyl or amino;

A' is a pyridinyl of the formula

$$R^{\underline{k}} - A^{\underline{l}} - \underbrace{}_{\underline{k}}$$

optionally substituted by one or more R^k selected from the group consisting of hydroxy, alkyl, alkoxy, alkoxyalkyl, thioalkyl, haloalkyl, cyano, amino, alkylamino, halogen, acylamino, sulfonamide and -COR;

R is hydroxy, alkoxy, alkyl or amino;

with respect to Z^1 and Z^2 :

Z¹ is selected from the group consisting of CH₂, O, N, CO, S, SO, SO₂, CH and NR_k;

R_k is selected from H or lower alkyl;

 Z^2 is a 2 to 5 carbon linker optionally containing one or more heteroatom selected from the group consisting of O, S and N; or

 Z^1 - Z^2 contains a moiety selected from the group consisting of carboxamide, sulfone, sulfonamide, alkenylene, alkynylene, and acyl;

wherein the carbon and nitrogen atoms of Z^1 - Z^2 are optionally substituted by alkyl, alkoxy, thioalkyl, alkylsulfone, aryl, alkoxyalkyl, hydroxy, alkylamino, heteroaryl, alkenyl, alkynyl, carboxyalkyl, halogen, haloalkyl or acylamino;

wherein Z_2 - Z_1 is attached to the X_1 substituent; at the para or meta position relative to

OH

n is 0 to 2;

R° is selected from the group consisting of hydrogen; alkyl; halogen, hydroxy, nitro, alkoxy, amino, haloalkyl, aryl, heteroaryl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, thioalkyl, alkylamino, arylamino, alkylsulfonylamino, acyl, acylamino, sulfonyl, sulfonamide, allyl, alkenyl, methylenedioxy, ethylenedioxy, alkynyl, alkynylalkyl, carboxy, alkoxycarbonyl, carboxamido, cyano, and -(CH₂)_m COR;

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X' is selected from the group consisting of -O-, CO, SO₂, NR^m and (CHR^p)_q;

R[™] is H or alkyl;

R^p is H, alkyl; alkoxy or hydroxy;

q is 0 or 1;

with respect to X, X² and Y:

X² is selected from the group consisting of -CHR^e-, CO, SO₂, O, NR^f and S;

Rf is H or alkyl;

Re is selected from the group consisting of H, alkyl, hydroxy and alkoxy;

X or Y are independently selected from the group consisting of -CR⁸- or -N-wherein R⁸ is selected from the group consisting of H, alkyl, haloalkyl, fluoro, alkoxyalkyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkylsulfone, hydroxyalkyl, hydroxy, alkoxy, and carboxyalkyl; or

the group $X-X_2-Y$ contains a moiety selected from the group consisting of acyl, alkyl, amino, ether, thioether, sulfone and olefin;



forms a 3-8 membered monocyclic ring system; or an 8-11 membered bicyclic system; optionally saturated or unsaturated; the monocyclic ring system optionally containing 1-2 heteroatoms selected from N, O and S; the bicyclic ring system optionally containing or optionally containing the group such as SO₂ or CO; and cycloalkyl, optionally substituted with one or more substituent selected from the group consisting of alkyl, halogen, cyano, carboalkoxy, haloalkyl, alkoxyalkyl, alkylsulfone, aryl, heteroaryl, arakyl, heteroarakyl, or alkoxy; and

 R^b is X_3 - R^h wherein X_3 is selected from the group consisting of O, S and NR^j wherein R^h and R^j are independently selected from the group consisting of H, alkyl, acyl, aryl, aralkyl and alkoxyalkyl.

Claim 67 (Original) A compound according to claim 66 wherein

A¹ is selected from the group consisting of

$$Z^{a}$$
 and Z^{a} Z^{a}

Z^a is selected from the group consisting of H, alkyl, alkoxy, hydroxy, amine, alkylamine, dialkylamine, carboxyl, alkoxycarbonyl, hydroxyalkyl, halogen and haloalkyl; and

R¹ is selected from the group consisting of H, alkyl, alkoxyalkyl, acyl, haloalkyl, alkoxycarbonyl, pyridylamino, imidazolylamino, morpholinopyridine, tetrahydronaphthyridine, oxazolylamino, thiazolylamino, pyrimidinylamino, quinoline, isoquinoline, tetrahydroquinoline, imidazopyridine, benzimidazole, pyridone, and quinolone.

Claim 68 (Original) A compound according to claim 66 wherein

A¹ is selected from the group consisting of

X⁴ is selected from the group consisting of H, alkyl, branched alkyl, alkylamino, aloxyalkylamino, haloalkyl, thioalkyl, halogen, amino, alkoxy, aryloxy, alkoxyalkyl, hydroxy, cyano and acylamino;

X⁵ is selected from the group consisting of H, alkyl, branched alkyl, alkylamino, aloxyalkylamino, haloalkyl, thioalkyl, halogen, amino, alkoxy, aryloxy, alkoxyalkyl, hydroxy, cyano and acylamino;

X⁶ is selected from the group consisting of H, alkyl, halogen, alkoxy, hydroxy, and haloalkyl; and

R⁷⁹ is selected from the group consisting of hydroxy, alkoxy, alkyl and amino.

Claim 69 (Original) A compound according to the claim 66 wherein

the moiety A¹-Z² is selected from the group consisting of

X⁴ is selected from the group consisting of H, alkyl, branched alkyl, alkylamino, aloxyalkylamino, haloalkyl, thioalkyl, halogen, amino, alkoxy, aryloxy, alkoxyalkyl, hydroxy, cyano and acylamino;

 R^{80} is selected from the group consisting of hydroxy, alkoxy, alkyl and amino; R^{81} is selected from the group consisting of hydroxy, alkoxy, alkyl and amino; and R^{82} is selected from the group consisting of hydroxy, alkoxy, alkyl and amino.

Claim 70 (Currently Amended) A compound according to claim 66 wherein

 X_1 is $(CHR^p)_q$; wherein q = 0;

B is a 3-, 4-, or a 5-membered <u>cycloalkyl ring</u> obtained by combining $X-X_2-Y$;

A is a phenyl ring substituted with Re; and

n = 1

Claim 71 (Currently Amended) A compound according to claim 70,

$$A^{1}-Z_{2}-Z_{1}$$

wherein the ring B is a 3-membered ring cyclopropyl;

 $Y = CR^{g}$;

wherein R⁸ is selected from the group consisting of H, alkyl, haloalkyl, alkoxyalkyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkylsulfone, hydroxyalkyl, hydroxy, alkoxy, and carboxyalkyl;

A is a phenyl ring substituted with R°; and

 $R^b = OH$

Claim 72. (Original) A compound according to claim 71 wherein R^e is selected from the group consisting of

$$R^{83}$$
 R^{84} R^{85} R

---R⁹¹ and CH₂R⁹²;

R⁸³ is selected from the group consisting of H, alkyl, OMe, OH, and halogen;

X' is selected from the group consisting of CH2 and O;

R⁸⁴ is selected from the group consisting of H, alkyl, OMe, OH, and halogen;

R⁸⁵ is selected from the group consisting of H, alkyl, OMe, OH, and halogen;

X⁸ is selected from the group consisting of NH, NMe, O, and S;

R⁸⁶ is selected from the group consisting of H and Me;

R⁸⁷ is selected from the group consisting of H and Me;

R⁸⁸ is selected from the group consisting of H, alkyl, OMe, OH, and halogen;

R⁸⁹ is selected from the group consisting of H and Me;

B' is selected from the group consisting of O, SO2, S and CO;

R⁹⁰ is selected from the group consisting of alkyl and aryl;

R91 is selected from the group consisting of alkyl and aryl; and

R⁹² is selected from the group consisting of aryl and heteroayl.

Claim 73 (Currently Amended) A compound according to claim 71 wherein

A' is selected from the group consisting of

$$X^{9-N}$$
 and X^{94} and X^{94}

X⁹ is selected from the group consisting of H, alkyl, and acyl;

R⁹³ is selected from the group consisting of H, Me, OH and alkoxyalkyl; and

R⁹³ is selected from the group consisting of H, Me, OMe, and OH.

Claim 74 (Original) A compound according to claim 71 wherein

ring A is a phenyl ring; and

 Z_1 - Z_2 and X_1 -X are connected para to each other.

Claim 75 (Original) A compound according to claim 74 wherein the phenyl ring is optionally substituted with one or more substituents selected from the group consisting of alkyl; halogen, hydroxy, alkoxy, haloalkyl, aryl, heteroaryl, alkoxyalkyl, sulfonamide, methylenedioxy, ethylenedioxy, alkynyl, and alkynylalkyl.

Claim 76 (Original) A compound according to claim 74 wherein Z_1 is selected from the group consisting of CH_2 , O, NR_2 , CO, S, SO, and SO_2 .

Claim 77 (Original) A compound according to claim 74 wherein A¹ is selected from the group consisting of

Claim 78 (Currently Amended) A compound according to the claim 66,

$$A^{1}-Z_{2}-Z_{1}$$

wherein

 X^{1} is $(CHR^{p})_{q}$; wherein q = 0;

A is a phenyl ring substituted with R^c

B is a 3-member ring cyclopropyl obtained by combining $X-X_2-Y$;

n = 1; and

 R_m and R_n are selected from the group consisting of H, alkyl, halogen, alkoxy, haloalkyl, alkoxyalkyl, alkylsulfone, cyano, carboalkoxy, aryl, heteroaryl, aralkyl and heteroaralkyl; or

R_m and R_n may from form a spirocyclic ring system.

Claim 79 (Currently Amended) A compound according to the claim 78 wherein A¹ is

$$X^{9}$$
 And X^{9} and X^{9} X^{9} X^{9}

selected from the group consisting of

R⁹⁴ is selected from the group consisting of H, Me, OH, and alkoxyalkyl;

R⁹⁴ is selected from the group consisting of H, Me, OMe, and OH; and

Claim 80 (Original) A compound according to claim 66 selected from the group consisting of:

- 2-[4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid;
- 2-[4-[3-(2-pyridinylamino)propoxy]phenyl] cyclopentaneacetic acid;
- 3-[4-[3-(2-pyridinylamino)propoxy]phenyl] cyclopentaneacetic acid;
- 2,2-difluoro-3-[4-[3(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid
- (2-{4-[2-(5,6,7,8-Tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid;
- 2-[3-methyl-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid;
- 2-[2-methoxy-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid;
- 3-bromo-5-fluoro-••,• -dimethyl-4-[3-(2-pyridinylamino)propoxy]-benzene butanoic acid;
- 2-[2-methyl-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid;
- 3-fluoro-β, β-dimethyl-4-[3-(2-pyridinylamino)propoxy]benzene-butanoic acid;
- 3-chloro-β, β-dimethyl-4-[3-(2-pyridinylamino)propoxy]benzene-butanoic acid;
- 2-[3-fluoro-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid;
- 2-[2-fluoro-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid;
- β-methyl-β-[[4-[3-(2-pyridinylamino)propoxy]phenyl]methyl]-3-pyridine propanoic acid;
- 3-methoxy-β, β-dimethyl-4-[3-(2-pyridinylamino)propoxy]benzene-butanoic acid;
- 2-[4-[2-[6-(methylamino)-2-pyridinyl]ethoxy]phenyl]cyclopropane-acetic acid;
- 2-[4-[2-(3,4-dihydro-2*H*-pyrido[3,2-*b*]-1,4-oxazin-6-yl)ethoxy]phenyl]-cyclopropaneacetic acid;
- 3-[4-[3-(2-pyridinylamino)propoxy]phenyl]cyclobutaneacetic acid;
- (2-{2-Methoxy-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (2-{2-Fluoro-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (2-{2-Acetoxy-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Methyl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Methoxymethyl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Methanesulfonylmethyl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;

- (1-Pyridin-3-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Benzo[1,3]dioxole-5-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-(2,3-Dihydro-benzofuran-6-yl)-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Isoxazol-3-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Isoxazol-5-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Oxazol-5-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid;
- (2-{4-[3-(Pyridin-2-ylamino)-propoxy]-phenyl}-1-thiazol-5-yl-cyclopropyl)-acetic acid;
- (1-Pyridin-3-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid;
- (1-Methyl-2-{4-[2-(6-methylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid;
- (2-{4-[2-(6-Ethylamino-pyridin-2-yl)-ethoxy]-phenyl}-1-methyl-cyclopropyl)-acetic acid;
- [2-(4-{2-[6-(2-Methoxy-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-1-methyl-cyclopropyl]-acetic acid;
- [2-(4-{2-[6-(3-Methoxy-propylamino)-pyridin-2-yl]-ethoxy}-phenyl)-1-methyl-cyclopropyl]-acetic acid;
- (2-{4-[2-(6-Acetylamino-pyridin-2-yl)-ethoxy]-phenyl}-1-methyl-cyclopropyl)-acetic acid;
- [1-Methyl-2-(4-{2-[6-(2,2,2-trifluoro-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid;
- (2-{4-[2-(6-Ethylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- [2-(4-{2-[6-(2-Methoxy-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid;
- [2-(4-{2-[6-(2,2,2-Trifluoro-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid;
- [2-(4-{2-[6-(3-Methoxy-propylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid; and
- (2-{4-[2-(6-Acetylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid.

Claim 81 (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 66 and a pharmaceutically acceptable carrier.

Claim 82 (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 70 and a pharmaceutically acceptable carrier.

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Claim 83 (Original) A method for treating conditions mediated by the $\alpha_v \beta_3$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v \beta_3$ inhibiting amount of a compound of Claim 66.

Claim 84 (Original) A method for treating conditions mediated by the $\alpha_{\nu}\beta_{3}$ integrin in a mammal in need of such treatment compirising administering an effective $\alpha_{\nu}\beta_{3}$ inhibiting amount of a compound of Claim 70.

Claim 85 (Original) The method according to Claim 83 wherein the condition treated is tumor metastasis.

Claim 86 (Original) The method according to Claim 84 wherein the condition treated is tumor metastasis.

Claim 87 (Original) The method according to Claim 83 wherein the condition treated is solid tumor growth.

Claim 88 (Original) The method according to Claim 84 wherein the condition treated is solid tumor growth.

Claim 89 (Original) The method according to Claim 83 wherein the condition treated is angiogenesis.

Claim 90 (Original) The method according to Claim 84 wherein the condition treated is angiogenesis.

Claim 91 (Original) The method according to Claim 83 wherein the condition treated is osteoporosis.

Claim 92 (Original) The method according to Claim 84 wherein the condition treated is osteoporosis.

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Claim 93 (Original) The method according to Claim 83 wherein the condition treated is humoral hypercalcemia of malignancy.

Claim 94 (Original) The method according to Claim 84 wherein the condition treated is humoral hypercalcemia of malignancy.

Claim 95 (Original) The method according to Claim 83 wherein the condition treated is smooth muscle cell migration.

Claim 96 (Original) The method according to Claim 84 wherein the condition treated is smooth muscle cell migration.

Claim 97 (Original) The method according to Claim 83 wherein restenosis is inhibited.

Claim 98 (Original) The method according to Claim 84 wherein restenosis is inhibited.

Claim 99 (Original) The method according to Claim 83 wherein atheroscelorosis is inhibited.

Claim 100 (Original) The method according to Claim 84 wherein atheroscelorosis is inhibited.

Claim 101 (Original) The method according to Claim 83 wherein macular degeneration is inhibited.

Claim 102 (Original) The method according to Claim 84 wherein macular degeneration is inhibited.

Claim 103 (Original) The method according to Claim 83 wherein retinopathy is inhibited.

Claim 104 (Original) The method according to Claim 84 wherein retinopathy is inhibited.

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Claim 105 (Original) The method according to Claim 83 wherein arthritis is inhibited.

Claim 106 (Original) The method according to Claim 84 wherein arthritis is inhibited.

Claim 107 (Original) A method for treating conditions mediated by the $\alpha_v \beta_s$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v \beta_s$ inhibiting amount of a compound of Claim 66.

Claim 108 (Currently Amended) A method for treating conditions mediated by the $\alpha_v \beta_s$ integrin in a mammal in need of such treatment empirising comprising administering an effective $\alpha_v \beta_s$ inhibiting amount of a compound of Claim 70.

Claim 109 (Currently Amended) The method according to Claim 107 wherein the condition treated is $\alpha_{\nu}\beta_{\nu}$ mediated-tumor metastasis.

Claim 110 (Currently Amended) The method according to Claim 108 wherein the condition treated is $\alpha_v \beta_s$ mediated-tumor metastasis.

Claim 111 (Currently Amended) The method according to Claim 107 wherein the condition treated is $\alpha_v \beta_v$ mediated-solid tumor growth.

Claim 112 (Currently Amended) The method according to Claim 108 wherein the condition treated is $\alpha_v \beta_v$ mediated-solid tumor growth.

Claim 113 (Original) The method according to Claim 107 wherein the condition treated is angiogenesis.

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Claim 114 (Original) The method according to Claim 108 wherein the condition treated is angiogenesis.

Claim 115 (Original) The method according to Claim 107 wherein the condition treated is osteoporosis.

Claim 116 (Original) The method according to Claim 108 wherein the condition treated is osteoporosis.

Claim 117 (Original) The method according to Claim 107 wherein the condition treated is humoral hypercalcemia of malignancy.

Claim 118 (Original) The method according to Claim 108 wherein the condition treated is humoral hypercalcemia of malignancy.

Claim 119 (Original) The method according to Claim 107 wherein the condition treated is smooth muscle cell migration.

Claim 120 (Original) The method according to Claim 108 wherein the condition treated is smooth muscle cell migration.

Claim 121 (Original) The method according to Claim 107 wherein restenosis is inhibited.

Claim 122 (Original) The method according to Claim 108 wherein restenosis is inhibited.

Claim 123 (Original) The method according to Claim 107 wherein atheroscelorosis is inhibited.

Claim 124 (Original) The method according to Claim 108 wherein atheroscelorosis is inhibited.

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Claim 125 (Original) The method according to Claim 107 wherein macular degeneration is inhibited.

Claim 126 (Original) The method according to Claim 108 wherein macular degeneration is inhibited.

Claim 127 (Original) The method according to Claim 107 wherein retinopathy is inhibited.

Claim 128 (Original) The method according to Claim 108 wherein retinopathy is inhibited.

Claim 129 (Original) The method according to Claim 107 wherein arthritis is inhibited.

Claim 130 (Original) The method according to Claim 108 wherein arthritis is inhibited.